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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,856	07/10/2006	Stefan Ludwig	7003/45	6403

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EXAMINER	
HA, JULIE	
ART UNIT	**PAPER NUMBER**
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,856	LUDWIG ET AL.	
	Examiner	Art Unit	
	Julie Ha	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-21* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group 1, claim(s) 3-4, drawn to a method for the prophylaxis or therapy of at least one viral disease, comprising administering the active substance has the core sequence DEVD.

Group 2, claim(s) 3-4, drawn to a method for the prophylaxis or therapy of at least one viral disease, comprising administering the active substance has the core sequence DMQD.

Group 3, claim(s) 3-4, drawn to a method for the prophylaxis or therapy of at least one viral disease, comprising administering the active substance has the core sequence DQMD.

Group 4, claim(s) 3-4, drawn to a method for the prophylaxis or therapy of at least one viral disease, comprising administering the active substance has the core sequence LEHD.

Group 5, claim(s) 3-4, drawn to a method for the prophylaxis or therapy of at least one viral disease, comprising administering the active substance has the core sequence LETD.

Group 6, claim(s) 3-4, drawn to a method for the prophylaxis or therapy of at least one viral disease, comprising administering the active substance has the core sequence ESMD.

Group 7, claim(s) 3-4, drawn to a method for the prophylaxis or therapy of at least one viral disease, comprising administering the active substance has the core sequence IETD.

Group 8, claim(s) 3-4, drawn to a method for the prophylaxis or therapy of at least one viral disease, comprising administering the active substance has the core sequence AEVD.

Group 9, claim(s) 3-4, drawn to a method for the prophylaxis or therapy of at least one viral disease, comprising administering the active substance has the core sequence VAD.

Group 10, claim(s) 3-4, drawn to a method for the prophylaxis or therapy of at least one viral disease, comprising administering the active substance has the core sequence LEVD.

Group 11, claim(s) 3-4, drawn to a method for the prophylaxis or therapy of at least one viral disease, comprising administering the active substance is a non-peptide inhibitor of caspases.

Group 12, claim(s) 3-4, drawn to a method for the prophylaxis or therapy of at least one viral disease, comprising administering the active substance is dominant-negative mutant of a caspase.

Group 13, claim(s) 3-4, drawn to a method for the prophylaxis or therapy of at least one viral disease, comprising administering the active substance is an antisense-oligonucleotide.

Group 14, claim(s) 3-4, drawn to a method for the prophylaxis or therapy of at least one viral disease, comprising administering the active substance is a protein comprising the cellular inhibitors of apoptosis proteins cIAP1, cIAP2, the X-linked inhibitor of apoptosis protein XIAP, antiapoptotic protein Bcl-2 or baculoviral protein p35.

Group 15, claim(s) 3-4, drawn to a method for the prophylaxis or therapy of at least one viral disease, comprising administering the active substance is dsRNA oligonucleotide.

Group 16, claim(s) 3-4, drawn to a method for the prophylaxis or therapy of at least one viral disease, comprising administering the active substance is an antibody or antibody fragment specific for a caspase or a fusion protein.

Group 17, claim(s) 5-8, drawn to a combination preparation comprising at least two antiviral active substances, wherein at least one antiviral active substance is selected from the active substances.

Group 18, claim(s) 9-13, drawn to a test system for finding active substances comprising caspase-3.

Group 19, claim(s) 14, drawn to a method for identifying at least one active substance for the prophylaxis or therapy of viral diseases, comprising the following steps: a) bringing at least one test system into contact with at least one potential active substance, and b) determining the effects on virus multiplication.

Group 20, claim(s) 15, drawn to a method for preparing a drug for the prophylaxis or therapy of viral disease, comprising the following steps: a) performing a test system, and b) reacting the active substance(s) with at least one auxiliary and/or additional substance.

Group 21, claim(s) 16-17 and 20, drawn to a method for the prophylaxis or therapy of a viral infection comprising an infection with an influenza infection, comprising administering a physiologically effective dose of a pharmaceutical composition, comprising at least one caspase inhibitor, caspase-3 inhibitor.

Group 22, claim(s) 18-19, drawn to a combination preparation comprising at least one caspase inhibitor and another antiviral active substance, which is not a caspase inhibitor, comprising an inhibitor of one or several cellular kinases, and galenic auxiliary and carrier substances, wherein the caspase inhibitor and the further antiviral active substance exist in a mixture or in separate galenic preparations.

Group 23, claim(s) 21, drawn to a method for screening for prospective antiviral active substances, comprising the steps a) to e).

PLEASE NOTE: It is noted that claim 20 recite the language "use of a combination preparation." "Use" claim language is improper under U.S. practice. Thus, for the purposes of this restriction, "use of a combination preparation" has been interpreted as a "method of use." Accordingly, claim 20 has been grouped separately with claims 16-17 (Group 21) from claims 18-19 as a method claim. Furthermore, it was unclear whether there was a typographical error in the claim language. The first line of the claim recites, "The use or a combination preparation according to claim 18..." It was unclear if the "or" was meant to be an "of" or if the Applicant meant "the use or a combination preparation" as recited. If claim 20 is amended to recite the combination preparation as claims 18-19, and Group 22 is elected, then claim 20 will be rejoined later with Group 22 at the time of First Office action.

Linking Claim

2. Claims 1-2 link(s) inventions 1 through 16. The restriction requirement among

the linked inventions is **subject to** the nonallowance of the linking claim(s), claims 1-2.

Upon the indication of allowability of the linking claim(s), the restriction requirement as to the linked inventions **shall** be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104 **Claims that require all the limitations of an allowable linking claim** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

3. Applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, the allowable linking claim, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

4. The inventions listed as Groups 1-24 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The active substance that are peptide and non-peptide inhibitors are distinct because the structures are different. The peptide sequences are different and therefore, each sequence is structurally distinct. There is no common structure present. For example, peptide sequence DEVD is patentably independent and distinct from peptide sequence LEHD or LETD; peptide sequence ESMD is patentably independent and distinct from Peptide sequence IETD or AEVD. There is no common structure among these peptides. Further, search for one would not lead to the other. Furthermore, an antisense-oligonucleotide, dsRNA and an antibody or antibody fragments are patentably independent and distinct from peptide inhibitors. There is no common core structure

among the groups because they all have different structures. For example, peptides have peptide linkages and an amide and carboxyl groups, while oligonucleotides have heterocyclic base, a sugar and phosphate groups.

5. The situation involving the so-called Markush practice wherein a single claim defines alternatives (chemical or non-chemical) is also governed by PCT Rule 13.2. In this special situation, the requirement of a technical interrelationship and the same or corresponding special technical features as defined in PCT Rule 13.2, shall be considered to be met when the alternatives are of a similar nature.

6. When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled:

(A) All alternatives have a common property or activity; and

(B)

(1) A common structure is present, i.e., a significant structural element is shared by all of the alternatives; or

(B)

(2) In cases where the common structure cannot be the unifying criteria, all alternatives belong to a recognized class of chemical compounds in the art to which the invention pertains.

7. In paragraph (B)(1), above, the words "significant structural element is shared by all of the alternatives" refer to cases where the compounds share a common chemical structure which occupies a large portion of their structures, or in case the compounds have in common only a small portion of their structures, the commonly shared structure constitutes a structurally distinctive portion in view of existing prior art, and the common structure is essential to the common property or activity. The structural element may be a single component or a combination of individual components linked together.

8. In paragraph (B)(2), above, the words "recognized class of chemical compounds" mean that there is an expectation from the knowledge in the art that members of the class will behave in the same way in the context of the claimed invention. In other words, each member could be substituted one for the other, with the expectation that the same intended result would be achieved.

Species Election

9. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

Different cellular caspases;

Different antiviral active substances: from claim 3;

Different antiviral active substance which is not caspase inhibitors from claim 20;

Non-peptide inhibitor of caspases;

Dominant-negative mutant of a caspase;

An antisense-oligonucleotide

A protein that acts as caspase inhibitors: CIAP1, cIAP2, XIAP, Bcl-2 or p35;

dsRNA oligonucleotide;

antibody or antibody fragment;

Different viral diseases;

Different kinase inhibitor;

Different antivirally acting substance: 1-adamantamine, a rimantadine, a neuraminidase inhibitor, or nucleoside analog comprising ribavirin;

Different neuraminidase inhibitors;

Different inhibitor of cellular kinases;

Different virus infecting the cell;

Different types of cells.

10. Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

11. If one group from Groups 1-16 is elected, Applicant is required to elect a single disclosed species of viral disease. Furthermore, if an election is made from Groups 11-16, Applicant is further required to elect a single disclosed species of non-peptide inhibitor or caspases (for Group 11), a single disclosed species of dominant-negative mutant of a caspase (for Group 12), a single disclosed species of an antisense-oligonucleotide (for Group 13), a single disclosed species of a protein (i.e., cIAP1, cIAP2, X-linked inhibitor of apoptosis protein XIAP, Bcl-2 or p35) (for Group 14), a single disclosed species of dsRNA oligonucleotide (for Group 15), a single disclosed species of an antibody or antibody fragment (for Group 16). If Group 17 is elected, Applicant is required to elect a single combination preparation for the prophylaxis or therapy, comprising at least two antiviral active substances. This means, that the Applicant is required to elect the combination composition: for example, Applicant elects a combination preparation comprising Z-DEVD-FMK and ZX-LE(OMe)TD(OMe)-FMK or Applicant elects a combination preparation comprising Z-DEVD-FMK and another disclosed antiviral active agent (such as from claim 7). This is only an example, and the Applicant can elect any disclosed combination preparation. Furthermore, Applicant is required to elect a single disclosed viral infecting and a single disclosed kinase inhibitor. If Group 18 is elected, Applicant is required to elect a single disclosed species of cellular caspase, at least one virus infection the cells and the type of cell (a single disclosed type of cells). If Group 19 is elected, Applicant is required to elect a single disclosed species of viral disease, the test system (i.e., cell, virus infecting the cells, cellular caspase), and active substance (such as Z-DEVD-FMK). If Group 20 is elected,

Applicant is required to elect a single disclosed species of viral disease, test system (i.e., cell, virus infecting the cells, cellular caspase), and if there is an additional substance (what that substance is). If Group 21 is elected, Applicant is required to elect a single disclosed species of a pharmaceutical composition comprising at least one caspase inhibitor, caspase-3 inhibitor. For example, Applicant elects a composition comprising Z-DEVD-FMK only, then the invention will be examined only on the compound elected. For example, Applicant elects a composition comprising Z-DEVD-FMK and an antiviral active substance, which is not a caspase inhibitor (i.e. inhibitors of cellular kinases from claim 20). In this case, Applicant also needs to elect a single disclosed species of inhibitor of cellular kinase. If Group 22 is elected, Applicant is required to elect a single disclosed species of a combination preparation comprising at least one caspase inhibitor and another antiviral active substance, which is not a caspase inhibitor comprising an inhibitor of cellular kinase (from claim 20 for example?). If Group 23 is elected, Applicant is required to elect a single disclosed species of a cell containing a caspase, an active substance or a mixture of active substances, and viral infection infecting the cell.

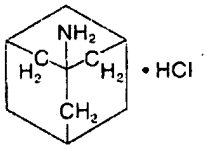
12. Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

13. The claims are deemed to correspond to the species listed above in the following manner:

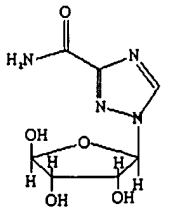
3 in part, 4, 7, 8, 10 and 20.

The following claim(s) are generic: Claims 1-2, 3 in part, 5-6, 9, 11-19 and 21.

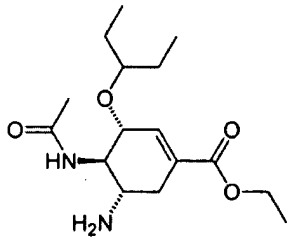
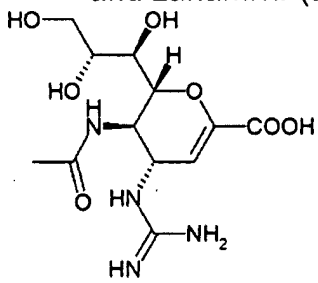
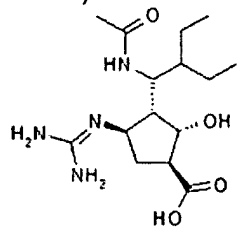
14. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: The antiviral active substances are patentably independent and distinct because the peptide content or in case on non-peptide inhibitors, due to different structures. The peptides have different sequences and therefore lead to a different structure. Search for DEVD sequence would not lead to peptide LEHD and so on. Non-peptide inhibitors of caspases, dominant-negative mutant of caspases, an antisense-oligonucleotide, a protein inhibitors (xIAP1, cIAP2, Bcl-2, etc), dsRNA oligonucleotides, and antibody or antibody fragment are patentably independent and distinct due to different structures. There is no common core structure among the groups because they all have different structures. For example, peptides have peptide linkages and an amide and carboxyl groups, while oligonucleotides have heterocyclic base, a sugar and phosphate groups. Further, search for one would not lead to the other. Different viral diseases are patentably independent and distinct because of the cells that they attack and different symptoms. For example, HIV is a viral disease caused by RNA, and this would have different symptoms from influenza virus and other viruses, such as rhinovirus or herpes virus. Further, search for one would not necessarily lead to the other. Different kinase inhibitors are patentably independent and distinct due to different structures. There are different types of inhibitors, for example, tyrosine kinase inhibitors, MAP kinase inhibitors, protein kinase inhibitors. These all have different structures and target different kinases/proteins. Different antiviral active substances 1-adamantamine, a rimantadine, a neuraminidase inhibitor, or nucleoside analog comprising ribavirin are patentably independent and distinct due to different structures. For example, 1-



adamantanamine has the structure where as a ribavirin has the structure



. Further, search for one would not lead to the other. Different neuraminidase inhibitors are patentably independent and distinct due to their structural

differences. For example, Oseltamivir is a type of neuraminidase inhibitor and has a structure  and zanamivir (another type of neuraminidase inhibitor) has the structure  and peramivir has the structure  . Further, search for one would not necessarily lead to the other. Different inhibitors of cellular kinases are patentably independent and distinct due to their different specificity and different structures. For example, a search for A MAP kinase inhibitor would not necessarily lead to an inhibitor for tyrosine kinase inhibitor. Different virus infecting the cells, as described above, are patentably independent and distinct because they attack different cells differently and the have different symptoms. For example, HIV is a viral disease caused by RNA, and this would have different symptoms from influenza virus and other viruses, such as rhinovirus or herpes virus. Further, search for one would not necessarily lead to the other. Different types of cells are patentably independent and distinct because the cells are from different origin. For example, Caco-2 cells are mature intestinal cells, while T84 cells are epithelial human colon carcinoma. Further, search for one would not necessarily lead to the other.

15. Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

16. The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

17. **Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.**

18. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Conclusion

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Julie Ha whose telephone number is 571-272-5982. The examiner can normally be reached on Mon-Fri, 8:00 am to 4:30 pm.

20. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

21. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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12/6/09
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